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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/765,086	01/17/2001	Erkki I. Ruoslahti	P-LJ 4575	6131

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EXAMINER	
YU, MISOOK	

ART UNIT	PAPER NUMBER
1642	13

DATE MAILED: 01/13/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/765,086	RUOSLAHTI ET AL.	
	Examiner	Art Unit	
	MISOOK YU, Ph.D.	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *14 October 2002* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-17* is/are pending in the application.

4a) Of the above claim(s) *1-7* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *8-17* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☒ The proposed drawing correction filed on _____ is: a)☐ approved b)☒ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

Election/Restrictions

This application contains claims 1-7 drawn to an invention nonelected with traverse in Paper No. 9. A complete reply to the final rejection must include cancelation of nonelected claims or other appropriate action (37 CFR 1.144) See MPEP § 821.01.

Claims 1-7 remain withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention.

Claims 1-17 are pending and claims 8-17 are examined on merits.

Drawings

The proposed drawing correction and/or the proposed substitute sheets of drawings, filed on October 4, 2001 have been considered. The substance of the changes is acceptable to the Examiner, and the changes would obviate the objection to the specification. However, the response does not meet the formal requirements for a proposed drawing correction, because it was not filed as a separate paper and because it was not in the form of a pen-and-ink sketch showing changes in red ink or with the changes otherwise highlighted. See MPEP § 608.02(v).

INFORMATION ON HOW TO EFFECT DRAWING CHANGES

1. Correction of Informalities -- 37 CFR 1.85

New corrected drawings must be filed with the changes incorporated therein. Identifying indicia, if provided, should include the title of the invention, inventor's name, and application number, or docket number (if any) if an application number has not been assigned to the application. If this information is provided, it must be placed on the front of each sheet and centered within the top margin. If corrected drawings are required in a Notice of Allowability (PTOL-37), the new drawings **MUST** be filed within the **THREE MONTH** shortened statu-tory period set for reply in the "Notice of Allowability." Extensions of time may NOT be obtained under the provisions of 37 CFR 1.136 for filing the corrected drawings after the mailing of a Notice of Allowability. The drawings should be filed as a separate paper with a transmittal letter addressed to the Official Draftsperson.

2. Corrections other than Informalities Noted by Draftsperson on form PTO-948.

All changes to the drawings, other than informalities noted by the Draftsperson, **MUST** be made in the same manner as above except that, normally, a highlighted (preferably red ink) sketch of the changes to be incorporated into the new drawings **MUST** be approved by the examiner before the application will be allowed. No changes will be permitted to be made, other than correction of informalities, unless the examiner has approved the proposed changes.

Timing of Corrections

Applicant is required to submit acceptable corrected drawings within the time period set in the Office action. See 37 CFR 1.185(a). Failure to take corrective action within the set (or extended) period will result in **ABANDONMENT** of the application.

Claim Rejections - 35 USC § 103

Claim 8, and 13 **remain rejected** for the reasons set forth in the previous office action under 35 U.S.C. 103(a) as being unpatentable over Arap et al (16 January 1998, Science Vol. 279, 377-380), Fossa et al (1997, European urology 31 Suppl 3 p3-8, abstract only), and US Pat. 5,789,542 (IDS, 4 August, 1998), and WO 90/12866 (01 November, 1990), Javadpour et al (IDS, 1996, J. med. Chem. Vol. 39, 3107-3113), Bessalle et al (IDS, 1990, FEBS Lett. 274, 151-155) and Alvarez-Bravo et al (IDS, 1994, Biochem. J. 302, 535-538).

Claim 8, and 13 are interpreted as drawn to method for delivering useful peptides to prostate tissue and selectively inducing apoptosis in prostate tissue using a chimera comprising a prostate-targeting peptide and an antimicrobial peptide.

Applicant argues that Arap et al or any other cited reference teaches or suggests the prostate homing part of the chimera. This and other arguments have been fully considered but found not persuasive because Arap et al teach method of selecting tissue-specific peptides by in vivo panning using phage display libraries. One in ordinary skill in art would have been motivated to find peptides specially targeting prostate since Fossa et al teach a great need to treat prostate cancer without generalized side effect caused by chemo and other currently available anti-cancer therapy. Further, one in ordinary skill would have been able to select peptides capable

of specifically binding to prostate following the teachings of Arap et al with a reasonable expectation of success at the time the instant application was filed. Note prostate-homing SMSIARL (identical to the instant SEQ ID NO:207) taught by WO 99/46284 (cited below for the rejection of claims 9 and 14). Applicant further argues that WO 90/12866 teaches away from the claimed invention because the antimicrobial peptide described in the reference is cytotoxic to cancer cells only but not normal tissue. This argument is not convincing because the instant specification mainly talks about the instant invention as cancer treatment, not inducing apoptosis in normal prostate tissue. Note especially the abstract and Field of the Invention of the instant specification. Applicant argues that there is no motivation since the preamble of the instant claim is now amended to directing the chimera to prostate tissue instead of to prostate cancer. However, cancerous prostate tissue is also prostate tissue and one in ordinary skill would have been motivated to find a peptide capable of recognizing only prostate tissue because this property can be used selectively direct antimicribial peptides to prostate tissue only, thereby selectively inducing apoptosis of abnormally proliferating prostate cells without causing generalized side effects.

Claims 9, 14 **remain rejected** under 35 U.S.C. 103(a) as being unpatentable over Arap et al (16 January 1998, Science Vol. 279, 377-380), Fossa et al (1997, European urology 31 Suppl 3 p3-8, abstract only), and US Pat. 5,789,542 (IDS, 4 August, 1998), and WO 90/12866 (01 November, 1990), Javadpour et al (IDS, 1996, J. med. Chem. Vol. 39, 3107-3113), Bessalle et al (IDS, 1990, FEBS Lett. 274, 151-155) and Alvarez-Bravo et al (IDS, 1994, Biochem. J. 302, 535-538) as applied to claims 8, 13, and 18 above, and further in view of WO 99/46284 (IDS).

The claims are drawn to method directing an antimicrobial peptide to prostate and selectively inducing apoptosis in prostate tissue with a chimera comprising SEQ ID NO: 207 as prostate-targeting peptide and antimicrobial peptide.

Applicant argues that antimicrbimal part of the chimera is not obvious over WO 99/46284. However, this argument is not convincing because US Pat. 5,789,542, WO 90/12866, Javadpour et al (IDS, 1996, J. med. Chem. Vol. 39, 3107-3113), or Alvarez-Bravo et al (IDS, 1994, Biochem. J. 302, 535-538) all teach antimicrobial peptides and it

would been obvious to attach the antimicrobial peptides taught by the prior art to the prostate homing peptide taught by WO 99/46284 and also obvious to selectively direct the chimeria to prostate with reasonable expectation of success to kill prostate cancer cells without causing generalized side effects.

Claims 10, and 15 **remain rejected** under 35 U.S.C. 103(a) as being unpatentable over Arap et al (16 January 1998, Science Vol. 279, 377-380), Fossa et al (1997, European urology 31 Suppl 3 p3-8, abstract only), and US Pat. 5,789,542 (IDS, 4 August, 1998), and WO 90/12866 (01 November, 1990), Javadpour et al (IDS, 1996, J. med. Chem. Vol. 39, 3107-3113), Bessalle et al (IDS, 1990, FEBS Lett. 274, 151-155) and Alvarez-Bravo et al (IDS, 1994, Biochem. J. 302, 535-538) as applied to claims 8, 13, and 18 above, and further in view of Ellerby et al (IDS, September 1999, Nature Medicine 5, 1032-1038), Bessalle et al (IDS, 1990, FEBS Lett. 274, 151-155) and Alvarez-Bravo et al (IDS, 1994, Biochem. J. 302, 535-538), Javadpour et al (IDS, 1996, J. med. Chem. Vol. 39, 3107-3113).

Claims 10, and 15 are drawn to method directing all D-enantiomer of SEQ ID NO:200 to prostate and method of selectively inducing apoptosis in prostate tissue with a chimera comprising prostate-targeting peptide and all-D enantiomer of SEQ ID NO:200.

Applicant argues that the prior art does not teach or suggest chimeric prostate-homing peptides, nor provide any motivation for making such a chimeric peptide. These and other arguments have been fully considered but found unpersuasive because the prior art (especially Arap et al) teaches it is possible to select peptides capable specifically binding to endothelium of a solid tumor and based on this knowledge one in ordinary skill would have been motivated to find a peptide only able to target prostate tissue in order to attach cytotoxic moiety to selectively causes apoptosis in prostate cancer without damaging other tissues, thereby minimizing unnecessary side effect. Further, one in ordinary skill would have been able to select prostate homing peptide as demonstrated by WO 99/46284 (cited supra) at the time instant application was filed. In summary, the prior art teaches the first (i.e. the prostate-homing peptide) and the second (i.e., the all D-enantiomer of SEQ ID NO:200) parts of the chimera. Therefore, it

would have been obvious to one having ordinary skill in the art at the time the claimed invention was made to use the chimera for selectively induce apoptosis in prostate tissue, especially abnormally proliferating prostate cells with reasonable expectation of success.

Claims 11, 12, 16, and 17 **remain rejected** under 35 U.S.C. 103(a) as being obvious over WO 99/46284 above as applied to claims 9, 14, 19 and Ellerby et al above as applied to claims 10, 15, and 20, further in view of Arap et al (16 January 1998, Science Vol. 279, 377-380), Fossa et al (1997, European urology 31 Suppl 3 p3-8, abstract only), and US Pat. 5,789,542 (IDS, 4 August, 1998), and WO 90/12866 (01 November, 1990), Javadpour et al (IDS, 1996, J. med. Chem. Vol. 39, 3107-3113) as applied to Claim 8, 10, 13, 15, 18, and 20.

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Claims 11, 12, 16, and 17 are drawn to method directing a chimera SIARL-GG-d(KLAKLAK)2 to prostate and method of selectively inducing apoptosis in prostate tissue with the chimera.

Applicant argues the currently pending claims are not directed to cancer treatment but this argument is not persuasive because the prior art teaches that the chimera might be useful in selectively causing apoptosis in prostate cancer cells, thereby treating prostate cancer without causing severe generalized side effects. WO 99/46284 teaches the prostate-homing part of the specific chimera and Ellerby et al teaches the cancer-killing part of the microbial peptide, and the coupling domain of GG in Fig. 1 and the rest of the references teaches why it would have been obvious to one having ordinary skill in the art at the time the claimed invention was made to motivated to make the chimera shown in the claims to treat prostate cancer.

Conclusion

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not

mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to MISOOK YU, Ph.D. whose telephone number is 703-308-2454. The examiner can normally be reached on 8 A.M. to 5:30 P.M., every other Friday off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anthony C Caputa can be reached on 703-308-3995. The fax phone numbers for the organization where this application or proceeding is assigned are 703-305-3014 for regular communications and 703-872-9307 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Misook Yu
January 8, 2003

MARY E. MOSHER
PRIMARY EXAMINER
GROUP 1800